UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,966	07/28/2003	Laura P. Hale	1579-852	2269

23117 7590 06/26/2007
NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
REDDIG, PETER J	
ART UNIT	**PAPER NUMBER**
1642	

MAIL DATE	DELIVERY MODE
06/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,966	HALE, LAURA P.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,6 and 8-13* is/are pending in the application.

4a) Of the above claim(s) *4 and 8-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,6,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/9/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed April 12, 2007 in response to the Office Action of January 12, 2007 is acknowledged and has been entered. Applicant has elected the species A-2, patient suffers from a disorder associated with acquired proliferation of melanocytes and hyperpigmentation results from sun-exposure for examination. Because applicant did not distinctly and specifically point out any supposed errors in the restriction requirement, the election has been treated as an election without traverse MPEP 818.03(a).

2. In the November 9, 2006 response to the Office Action of August 9, 2006 previously pending claims 1, 3, 5, and 7 were cancelled, claims 2 and 6 were amended and new claims 12 and 13 were added. Claims 4 and 8-11 remain withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

3. Claims 2, 6, 12 and 13 are currently are being examined.

4. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2 and 6 remain rejected and new claims 12 and 13 are rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Office Action August 9, 2006, pages 3-9.

6. Applicant has provided arguments regarding the difference between in vitro cultured cells and in vivo host animals. Applicant argues that Freshney admittedly points out general differences between behavior of cultured cells and the counterparts in vivo. Applicants argue that

Freshney also states "Although the existence of such differences cannot be denied, it must be emphasized that many specialized functions are expressed in culture and as long as the limits of the model are appreciated, it can become a very valuable tool" (page 4, right column, second full paragraph). Applicant argues that in citing Dermer (a reference from 1994), the Examiner appears to be contending that because Dermer states that, in his opinion, "cell lines in which cancer is usually studied are unsuitable for the job", there are no meaningful cell culture models. Such an assertion is clearly without merit. Applicant argues that in regard to Gura, this reference points up past problems in cancer drug discovery and includes a discussion of approaches being taken to develop better cancer models and the importance of defining molecular targets. Applicant argues that it is not clear from the Examiner's comments why Gura is relevant to the present invention, which is unrelated to cancer drug screening. Applicants argue that in rejecting the claims as non-enabled, the Examiner also contends that undue experimentation would be required to determine the amount of ZAG sufficient to inhibit melanin synthesis by topical administration of ZAG. Applicants argue that the Examiner cites Poortsmans and Lei et al. Applicant argues that the relevance of these references to the Examiner's point is not seen. Applicant argues that it would be a matter of routine for one skilled in the art to determine an appropriate amount of ZAG to be administered to the skin of a patient. Applicants argue that the amount selected would be that which provided the effect sought. No invention would be required to make that selection.

Applicant's arguments have been fully considered but they are not persuasive. Although there are meaningful cell culture models in which the limits of the model are appreciated, one of skill in the art cannot extrapolate the teachings of the specification to the enablement of

inhibiting melanin synthesis in the skin of a patient with ZAG because the limits of predictability extrapolating the in vitro findings taught in the specification to the in vivo uses claimed have not been established in the specification or the prior art of record for the reasons previously set forth. The citation of Gura supports the general unpredictability of extrapolating from in vitro studies to in vivo therapeutic uses in the art of therapeutic drug development. Furthermore, as new claim 13 is drawn to inhibiting melanin synthesis in a patient that suffers from acquired proliferation of melanocytes, which reads on treating cancerous melanocytes in vivo, the teachings of Gura in regard to the unpredictability of developing cancer therapeutics based on in vitro studies are directly relevant to the instant rejection. Furthermore, as previously set forth, Poortsman and Lei teach that ZAG is at high levels in the endogenous skin, thus one of skill in the art would not predictably expect that additional ZAG would have an effect on melanin synthesis in vivo given the presence of already high levels of ZAG in the skin which one would be expected to have already exerted any potential effects on melanin synthesis that ZAG might have. Given the above and given that neither the specification nor the art of record has established that the in vitro effects observed with ZAG on melanin synthesis predictably extrapolate to any in vivo system and no examples of in vivo treatment with topical treatment of ZAG have been presented, thus it would require undue experimentation for one of skill in the art to practice the method as claimed.

Applicant argues that the Examiner's attention is directed to the fact that the Example provided in the application is based, at least in part, on the use of a widely used model of melanocyte function, B16 melanoma cells (see page 7, lines 1-3). Applicant argues that the Examiner has offered nothing by way of evidence to indicate why this is not an appropriate

model system. Applicant argues that the indeed, submitted herewith are publications demonstrating the well-established nature of this model (see Jimenez-Cervantes et al, J. Cell Sci. 114:2335 (2001) (page 2339, last paragraph of Introduction) and validation of that model (Martinez-Esparza et al, Int. J. Biochem. Cell Biol. 33:971 (2001)). Applicant argues that the in addition, the Examiner's attention is directed to the fact that the Example also includes a description of the inhibition by ZAG of melanin synthesis by normal melanocytes (see page 19). As pointed out, these studies indicate that ZAG has similar effects on melanin production in both normal and malignant melanocytes.

Applicant's arguments have been fully considered but they are not persuasive because the claims are not directed to treating B16 melanoma cells and the previously cited of Dermer and Freshney provide ample evidence why effects in this system cannot be predictably extrapolated to in vivo therapies. The cited references are also drawn to in vitro studies and are not commensurate in scope with the claimed in vivo method of treatment with ZAG, thus the cited references are not found persuasive. Furthermore Jimenez-Cervantes teaches that further work will be needed to ascertain whether their findings can be extrapolated to normal melanocytes, see p. 2343, last paragraph. Although Applicant argues that ZAG inhibits melanin synthesis in normal melanocytes on p. 19, it is not clear from the specification how "normal" the melan-A cells are given that they appear to be a cultured cell line and would susceptible to the unpredictable nature extrapolating results from cell culture taught by Dermer and Freshney.

Applicant's arguments have not been found persuasive and the rejection is maintained.

7. All other objections and rejections recited the Office action of August 9, 2006 are withdrawn.

8. No claims allowed.

9. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

A reply under 37 CFR 1.113 to a final rejection must include the appeal form, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

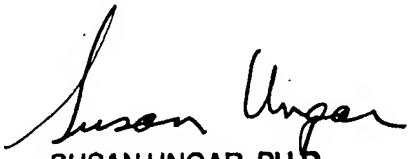
10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0890. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

PJR